CASE REPORT

Unexpected mild course of COVID-19 in HIV-positive patient with various risk factors: a case report

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and coronavirus disease 2019 (COVID-19) have been important factors leading to morbidity and mortality. Despite the emergence of new variants, such as Omicron, which can cause milder illness than e.g. Delta, there is a group of individuals at increased risk of severe COVID-19 and death as well as the development of long-lasting COVID-19, especially with various pre-existing comorbidities. It is surprising that some individuals with many co-morbidities and immune deficiency can have asymptomatic SARS-CoV-2 infection or mild COVID-19 without further complications, such as worsening of immune deficiency or inability to eradicate SARS-CoV-2, leading to persistent infection. Here, we present a case report of a mild clinical course of SARS-CoV-2 infection and its outcomes in a 71-year old, human immunodeficiency virus-positive patient with various comorbidities, such as hypertension, chronic kidney disease, insulin-dependent diabetes, hyperlipidemia, and obesity. SARS-CoV-2 infection was confirmed by polymerase chain reaction (PCR) test in August 2020. During that time, the patient did not report any additional complaints and remained in good general condition. The treatment for SARS-CoV-2 infection was symptomatic; the patient stayed at home, required no additional intervention nor hospitalization. After COVID-19, the patient suffered from deterioration of renal function, and was qualified for renal transplantation. At the time of writing of this article, the patient was 3 months post-transplantation, remaining in good general condition and professionally active.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease 2019 (COVID-19) are still important factors leading to morbidity and mortality. Despite new variants of infection, such as Omicron sub-types, which can cause milder illness than e.g. Delta, there is a group of individuals at increased risk of severe COVID-19 and death as well as the development of long-lasting COVID-19, with the risk increasing with age [1]. These individuals are those with various pre-existing health conditions, such as cardiovascular diseases, chronic kidney disease, diabetes, lung and liver diseases, obesity, immunodeficiency, disabilities, and

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mental health conditions [2]. A number of underlying diseases are associated with severe COVID-19. In Kompaniyets *et al.* [1] and Bucholc *et al.* [3] studies, based on follow-up of about 5,000 patients, hypertension and lipid metabolism disorders were found the most common risk factors for severe COVID-19 disease, while obesity, diabetes with complications, and anxiety disorders were the highest risk factors.

A retrospective cohort study among 167,500 COVID-19 patients living in Ontario, Canada, reported that solid organ transplantation, dementia, chronic kidney disease, severe mental illness, cardiovascular disease, hypertension, chronic obstructive pulmonary disease, cancer, diabetes, rheumatoid arthritis, human immunodeficiency virus (HIV), and asthma were associated with mortality or disease severity. The researchers highlighted that the number of comorbidities was a high-risk factor for death and serious outcomes [4]. Moreover, vaccination against COVID-19 cannot be sufficiently effective in individuals with immune suppression due to any reason [5-8].

It is well-known fact that Omicron sub-variants can evade immune response. For this reason, bi-valent vaccine is no longer recommended. The updated mono-valent (XBB-containing) COVID-19 mRNA vaccines manufactured by Moderna and Pfizer-BioNTech were authorized by the Food and Drug Administration (FDA) for emergency use in persons ≥ 6 months of age on September 11, 2023. The purpose of this new formula was to target more closely and efficiently currently circulating sub-variants of Omicron, and to improve the prevention of occurrence of severe course of COVID-19, hospitalization, and death [9]. These new vaccines are probably efficient also against the latest sub-variants, i.e., EG.5 and BA 2.86, which are more transmissible than previous sub-variants and could spread during the 2023/2024 season [9]. However, HIV-positive patients receiving antiretroviral therapy (ART), who have higher CD4+ T-cell counts respond efficiently to vaccinations against COVID-19, similar to healthy population. On the other hand, those with low CD4+ T-cell count can show reduced vaccine responses [10]. Moreover, preliminary results from a real-world experience study examining whether an extended interval between vaccine doses influences immune responses, observed that among frail, elderly individuals, prior SARS-CoV-2 infection and the type of mRNA vaccine affected antibody responses when administered with a 16-week interval between the doses. In these cohorts, homologous and heterologous use of mRNA vaccines was not associated with significant differences in antibody responses 4 weeks after the second dose, confirming their inter-changeability. Therefore, among elderly patients, it is important to maintain adequate intervals between vaccine doses [11].

Danwang *et al.* [12], in their systematic review and meta-analysis, investigated the risk of hospitalization, severe disease, and death in HIV-positive patients with COVID-19. Although their data indicated an increased risk of hospital admission comparing with HIV-negative individuals, no increased likelihood of developing severe COVID-19 and death was noted in unadjusted pooled analyses.

Overall, it is quite intriguing that some individuals with various co-morbidities and immune deficiency can have asymptomatic SARS-CoV-2 infection or mild course of COVID-19 without further complications, such as worsening of immune deficiency, inability to eradicate SARS-CoV-2, leading to persistent infection, and aggravation of organ function [13].

In the current paper, we present a case report of clinical course of SARS-CoV-2 infection and its outcomes in a HIV-positive patient with various risk factors for severe COVID-19.

Case report

A 71-year-old patient has been diagnosed with HIV infection in 2016. On admission to the outpatient department, he presented with multi-morbidity, including hypertension, chronic kidney disease, type 2 diabetes, hyperlipidemia, and obesity. He was treated with nebivolol, telmisartan, insulin, metformin, and statins. CD4+ T-cell count was 320/µl, HIV RNA of 47,000 copies/ml, creatinine of 1.42 mg/dl, and eGFR 50 ml/min. In June 2016, the patient started antiretroviral therapy with abacavir, lamivudine, and dolutegravir. Within 6 months, his viral load (VL) was below detection limit and CD4+ T-cell count reached 424/µl. Based on immunological and viral results, the patient remained on a stable efficient therapy.

In July 20218, he was admitted to outpatient hematology department due to fatigue, night sweats, and enlarged lymph nodes. Anemia was detected in lab tests. In August 2018, mixed cellularity classical Hodgkin's lymphoma Epstein-Barr virus-positive was diagnosed. Positron emission tomography (PET) scan revealed lymph node involvement on both sides of the diaphragm and splenomegaly. The treatment consisted of a total of 6 cycles ABVD chemotherapy scheme (adriblastin, bleomycin, vincristine, and dacarbazine), followed by X-ray radiotherapy with 26 Gy in 18 fractions for residual lesions. In control PET scan, there were no signs of active proliferation. Complete remission of the disease was achieved. The patient was two times vaccinated for COVID-19 with BNT162b2 mRNA vaccine in March and April 2020. However, in July 2020, he started to complain again of fatigue and weakness. Because of gradual exacerbation of the symptoms, hematological procedure was introduced for possible Hodgkin's lymphoma relapse, which was excluded. Additionally, there were no changes in CD4+ T-cell count and HIV VL. In August 2020, worsening of chronic kidney disease was observed in control lab test showing a significant decrease of estimated glomerular filtration rate (eGFR) and an increased level of creatinine (eGFR, 18 ml/min; creatinine 1.83 mg/dl). Antiretroviral therapy was adjusted. At the same time, SARS-CoV-2 infection was confirmed by PCR test. The treatment of SARS-CoV-2 infection was symptomatic, the patient remained at home, and required no additional intervention nor hospitalization. During follow-up, further deterioration of renal function was observed. The patient remained under continuous care of a nephrologist, hematologist, and infec-

tious disease specialist. Due to further deterioration of renal function in June 2021, it was decided to establish peritoneal dialysis access, and the patient started renal replacement therapy.

In March 2023, during hematology follow-up visit, the patient complained of lesion in his neck area. On physical examination, the lesion was firm, immovable relative to the ground, and not painful. In computed tomography (CT) scan of the neck region, a solid 4 cm × 3.2 cm lesion of unclear nature was found. Histopathological examination revealed bands of spindle cells without atypia, the cells showed no neural differentiation with low proliferative index. Antibiotic therapy was administered and after about 2 weeks, a withdrawal of the lesion was achieved.

Since the start of renal replacement therapy, the patient was supervised under the care of renal transplant clinic, and during that time, all procedures necessary to qualify the patient for renal transplant treatment were performed. At the time of writing of this article, the patient was 3 months after renal transplantation, remaining in generally good condition and professionally active.

Ethics and consent

The patient provided appropriate consent for his information to be shared and published in this case report. All procedures were carried out in accordance with ethical standards approved by the Wroclaw Medical University Review Board (approval number: KB – 208/2023).

Discussion

In the current paper, we described a 71-year-old HIV-positive patient, who suffered from various comorbidities, including obesity. All of these are considered risk factors for severe course of COVID-19, hospitalization, and death. Surprisingly, despite the above-mentioned information, the clinical course of the patient's SARS-CoV-2 infection was mild. In 2020, COVID-19 affected many individuals, leading to severe disease with subsequent complications and death [14]. In our patient, as a consequence of SARS-CoV-2 infection, serious health problems were anticipated. He experienced worsening of chronic kidney disease that was most likely associated with the infection, although HIV, diabetes, hypertension, lipid disorders, and Hodgkin's lymphoma therapy could influence his condition. There are much data indicating the impact of such comorbidities on kidney function [15-17]. Renal damage in hospitalized patients with SARS-CoV-2 co-infection is associated with an increased inpatient mortality and worse clinical course of the disease. From a pathophysiological point of view, COVID-19 is characterized by overproduction of inflammatory cytokines (IL-6, TNF-α), causing systemic inflammation and hypercoagulability. Available studies conclude that patients with chronic kidney disease treated conservatively or with renal replacement therapy are at higher risk of severe COVID-19 and death [18]. The question is: Despite so many risk factors, why did the patient have a mild type of the disease? In the presented patient, HIV infection was stable.

An analysis of 44 studies on SARS-CoV-2 infection with 38,971,065 COVID-19 patients reported a HIV prevalence rate of 26.9%, and it was higher in African countries. In further analysis, HIV-positive patients were most likely to be hospitalized due to COVID-19, while HIV was associated with an increased risk of death, but remarkably, it was not associated with the severity of the disease [12, 13].

The available data indicate the influence of HIV on SARS-CoV-2, of which spike glycoprotein is the centerpiece of the vaccine immunogen and therapeutic antibody construct that serves as a critical antigen in the evaluation of immune responses to COVID-19. A common feature of the enveloped viruses, such as SARS-CoV-2 and HIV-1, is the tendency to display host-derived glycans on entry proteins. There is a suggestion that anti-HIV broadly neutralizing antibodies can block the glycan envelope of the SARS-CoV-2 protein [19].

Another concept indicates correlation between high number of active CD8+ T-cells in patients with a mild course of COVID-19 treated efficiently with antiretroviral drugs [20].

Results of meta-analysis among 49,562 COVID-19 patients from 19 countries carried out by the COVID-19 Host Genetics Initiative showed the influence of genetic factors on COVID-19 course. The authors found 13 genome-wide significant loci associated with SARS-CoV-2 infection or severe COVID-19 [21]. In our patient, no genetic studies were performed.

One more explanation for the mild COVID-19 infection can be cross-reactive immunity to seasonal common coronaviruses and partially to SARS-CoV-2. These coronaviruses are responsible for frequent infections of the upper respiratory tract, occurring from fall to spring [21]. Moreover, previous vaccination against COVID-19 could prevent more severe courses of SARS-CoV-2 infections. An Italian study evaluated the immune response in people living with HIV/AIDS who have been vaccinated against COVID-19 to assess the role of HIV infection in the efficacy of vaccine. A high efficacy of COVID-19 mRNA vaccine in people living with HIV/AIDS was reported [22].

Finally, our patient was treated because of Hodgkin's lymphoma. Even though there was a few years gap between finishing lymphoma therapy and coronavirus infection, the weakened immune system could not respond adequately and fight the infection. In a multi-center study among 856 patients with lymphoma conducted by Italian researchers, anti-lymphoma treatment with anti-CD20-containing regimen had no effect on survival. Additionally, patients with Hodgkin's lymphoma showed more favorable survival rates, but this was partly related to a much younger age, and they were also treated more often in an out-patient clinic. The interval between lymphoma diagnosis and COVID-19 disease was inversely associated with mortality [23].

Conclusions

Currently, there is conflicting information available in the literature regarding the course of COVID-19 in people living with HIV/AIDS. Various studies, including cohort studies and case series, do not indicate an increased risk of SARS-CoV-2 infection or a more severe course of COVID-19 in people living with HIV/AIDS. There are also reports in the literature showing a beneficial effect of HIV medications or the infection itself on COVID-19. At the same time, other studies indicate an increased risk of severe COVID-19 disease progression, even in well-controlled HIV patients. It is not clear what exactly influences the course of SARS-CoV-2 infection in patients living with HIV; perhaps the multiple concomitant diseases found in these patients are important factors. Considering the above and analyzing the course of SARS-CoV-2 infection in the presented patient, it should be concluded that further studies among COVID-19 patients living with HIV are needed, contributing to better treatments of this disease. We assume that the course of COVID-19 depends of many factors, some of which are maybe complex and not yet investigated.

Disclosures

1. Institutional review board statement: This study was approved by the Wroclaw Medical University Review Board (approval number: KB – 208/2023).
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4. Conflicts of interest: None.

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